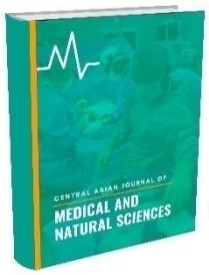
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 04 Issue: 06 | Nov-Dec 2023 ISSN: 2660-4159

http://cajmns.centralasianstudies.org

ANALYSIS OF THE SIGNIFICANCE OF POLYMORPHIC LOCUSES OF THE IL17A (rs2275913) AND IL17F (rs763780) GENE IN AUTOIMMUNE HEMOLYTIC ANEMIA

1. **Jakhonov A.Kh.**
2. **Matkarimova D.S.**
3. **Saidov A.**
4. **Boboev K.T.**

Received 20th Oct 2023,
Accepted 21st Nov 2023,
Online 25th Dec 2023

[1,2,3] Tashkent Medical Academy (Uzbekistan)
[4] Republican Specialized Scientific and Practical Medical Center of Hematology (Uzbekistan)

Abstract: Relevance. Autoimmune hemolytic anemia (AIHA), an acquired and relatively rare pathology in the entire group of hematological diseases, is characterized by the formation of autoantibodies, which in most cases leads to premature, in most cases intracellular, hemolysis of red blood cells.

Target. To study the features of the distribution of polymorphic loci of the IL17A (rs2275913) and IL17F (rs763780) genes in patients with AIHA, and also to determine their significance in the development of the disease and its severe course.

Methods and materials.The study included 93 adult patients (main group) diagnosed with autoimmune hemolytic anemia and 97 healthy donors (control comparison group) with no history of autoimmune diseases, matched by gender and age to the main group of patients.

Detection of the IL17A (rs2275913) and IL17F (rs763780) genetic polymorphisms was carried out by SNP-PCR using an Applied Biosystems 2720 (USA) programmable thermocycler using test systems from Litech (Russia) and Syntol (Russia).Statistical analysis of the results was carried out using the statistical software package “OpenEpi 2009, Version 9.3”.

Results.When assessing the nature of the differences in the distribution of alleles and genotypes of the cytokine polymorphic gene interleukin IL17A (rs2275913) in the main

group of patients with AIHA compared to healthy patients, it was found that carriers of a weakened allele (A) and genotypes are present are (G/A and A/A) is 2.1 times ($\chi2$=7.9; P=0.01), 1.8 times ($\chi2$=3.1; P=0, 1) and 6.6-fold ($\chi2$=3.9; p=0.1) increased risk for the formation of AIHA. P=0.05) as well as with an increased risk of formation of this form of AIHA by 3.0 times ($\chi2$=12.0; P=0.01), 2.2 times ($\chi2$=3.9 ; P=0.05) and 11.3-fold ($\chi2$). =6.9; P=0.01).

Statistical calculations of the distribution of polymorphic loci of the cytokine polymorphic gene interleukin IL-17F (rs763780) in patient groups compared to healthy patients made it possible to establish the presence of a tendency to increase the risk of developing AIHA in carriers of the mutant Arg allele almost twice as much ($\chi2$ = 2.7; P = 0.2) and His/Arg heterozygous carriers twice as much (20.4% versus 11.3%; $\chi2$ = 3.0; P = 0.1; OR = 2.0; CI: 0.91–4.45) and a trend toward a 2.2-fold ($\chi2$=3.0; P=0.1) and 2.4-fold ($\chi2$=3.3; P=0.1) increased risk for development, respectively severe AIHA when unfavorable alleles (Arg) and genotype (His/Arg) are carried, respectively.

Thus, the results show the possible contribution of the polymorphic genes IL17A (rs2275913) and IL-17F (rs763780) to the mechanisms of AIHA development and the development of severe diseases.

Key words: IL17A (rs2275913), IL-17F (rs763780), autoimmune hemolytic anemia, carriage, frequency, allele, genotype, risk of development, severe course.

Relevance. Autoimmune hemolytic anemia (AIHA), an acquired and relatively rare pathology in the entire group of hematological diseases, is characterized by the formation of autoantibodies, which in most cases leads to premature, in most cases intracellular, hemolysis of red blood cells [1, 3, 12] .

AIHA is of great medical and social importance due to the increasing number of severe and complicated forms of the disease [1, 3].

Nowadays, many aspects of the mechanisms of erythrocyte hemolysis in AIHA are quite well studied, proving its complexity [9]. Autoantibodies, the monocyte-macrophage system, complement systems and humoral and cellular immunity are particularly involved in the pathogenesis of the disease [6].

The interaction of all these relationships changes the activity of a number of pro-inflammatory cytokines, which overall leads to violations of immunological tolerance [14]. Meanwhile, the exact initial mechanisms that led to the start of this complex process are still not fully understood.

In this regard, the greatest interest of researchers is in studying the possible involvement of the host genetic component that plays a role in the regulation of cytokines [4, 16, 17].

One of the smartest representatives of the regulators of autoimmune processes are the interleukins 17A and 17F [2].

To date, there is no information on the study of the distribution characteristics and role of gene polymorphisms IL17A (rs2275913) and IL17F (rs763780) in AIHA in the Uzbek population, which served as the basis for the research.

Target. To study the features of the distribution of polymorphic loci of the IL17A (rs2275913) and IL17F (rs763780) genes in patients with AIHA, and also to determine their significance in the development of the disease and its severe course.

Methods and materials. The study included 93 adult (main group) patients with a diagnosis of autoimmune hemolytic anemia (mean age - mean age 41.2 ± 3.9 years), determined on the basis of clinical and laboratory changes, including the results of an antiglobulin test, as well as 97 healthy donors (control comparison group) without a history of autoimmune diseases, corresponding to the gender and age of the main patient group.

A random sampling method was used to select patients who applied for diagnostic examination and treatment at the Republican Specialized Scientific and Practical Medical Center of Hematology (RSNPMCG, Tashkent, Uzbekistan) during the period 2018 to 2022.

All examined patients were divided into groups: Group I – the main group of patients with AIHA (n=93); Group II – patients with mild AIHA (n=93); Group III – patients with moderate severity of AIHA (n=93); Group IV – patients with severe AIHA (n=93); Group V – control comparison group (n=97).

Informed consent was obtained from all study participants.

For molecular genetic studies, DNA was isolated from venous blood leukocytes according to the standard DNA isolation protocol. Detection of the IL17A (rs2275913) and IL17F (rs763780) genetic polymorphisms was carried out by SNP-PCR with an Applied Biosystems 2720 (USA) programmable thermal cycler using test systems from Litech (Russia) and Syntol (Russia), according to the study manufacturer's instructions. The specificity and quantity of the amplified fragments were checked by agarose gel electrophoresis.The statistical analysis of the results was carried out using the statistical software package “OpenEpi 2009, Version 9.3”. To assess the associative relationship between polymorphic allelic and genotypic variants of IL17A (rs2275913) and IL17F (rs763780) genes with the development of AIHA and its severe course, Fisher's exact test ($\chi 2$), reliability (P), odds ratios (OR) used and confidence intervals were calculated in groups of patients and healthy people (95% Cl).

Results and discussion. When investigating the prevalence of the IL17A (rs2275913) and IL17F (rs763780) polymorphic genes, we performed a comparative analysis of the agreement of the observed (Ho) frequencies with their expected (He) frequencies in groups of patients with AIHA and healthy patients -Vineyard Equilibrium (HW). The results showed that there were no significant differences between the genotype frequencies of the two polymorphic genes examined, indicating that the Ho and He frequencies corresponded to the canonical distribution ($p>0.05$).

The distribution results of the polymorphic IL17A gene (rs2275913) are shown in Table 1 (Table 1).

Table 1

The nature of the distribution of polymorphic loci of the polymorphism of the pro-inflammatory cytokine gene interleukin IL17A (rs2275913) in groups of patients with AIHA and healthy people.

Groups surveyed	Allele occurrence				Occurrence of genotypes					
	G		A		G/G		G/A		A/A	
	n	%	n	%	n	%	n	%	n	%
I main group AIHA, (n=93)	140	75.3	46	24.7	53	57.0	34	36.6	6	6.4
II – group AIHA with moderate course, (n=55)	88	80.0	22	20.0	35	63.6	18	32.7	2	3.7
Group III AIHA with severe course, (n=38)	52	68.4	24	31.6	18	47.4	16	42.1	4	10.5
IV – comparison group of healthy people, (n=97)	168	86.6	26	13.4	72	74.2	24	24.7	1	1.1

When assessing the significance of the differences in the transport of alleles and genotypes of the cytokine polymorphic interleukin gene IL17A (rs2275913) between the main group and the healthy group, it was found that in patients there was a statistically significant increase in the proportion of weakened A- alleles increased 2.1-fold (24.7% vs. 13.4%; $\chi 2 = 7.9$; P = 0.01; OR = 2.1; CI: 1.26–3.58) (Table 2).

Table **4.25**

Assessment of the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the pro-inflammatory cytokine interleukin IL17A (rs2275913) in the main group of patients with AIHA in relation to healthy people.

Alleles and genotypes	Number of alleles and genotypes in groups				χ^2	P	RR	95%CI	OR	95%CI
	Group I		Group IV							
	n	%	n	%						
G	140	75.3	168	86.6	7.9	0.01	0.9	0.57-1.32	0.5	0.28-0.8
A	46	24.7	26	13.4	7.9	0.01	1.2	0.61-2.17	2.1	1.26-3.58
G/G	53	57.0	72	74.2	6.3	0.03	0.8	0.44-1.33	0.5	0.25-0.84
G/A	34	36.6	24	24.7	3.1	0.1	1.5	0.84-2.6	1.8	0.94-3.27
A/A	6	6.5	1	1.0	3.9	0.05	6.3	3.22-12.2	6.6	1.02-42.9

Moreover, statistically significant differences were also determined in the carriage of the weakened homozygous A/A genotype, the frequency of which among patients with AIHA was 6.6 times higher than that among healthy people (6.5% versus 1.0%; $\chi2=3.9$; P=0.05; OR=6.6; CI : 1.02-42.9).

In addition, despite the fact that the differences between the groups for the main genotype G/G turned out to be less than one (57.0% versus 74.2%; $\chi2=6.3$; P=0.03; OR=0.5; CI: 0.25-0.84), however, in the ratio of heterozygote G/A among patients there was a clear tendency to increase it by 1.8 times (36.6% versus 24.7%; $\chi2=3.1$; P=0.1; OR=1.8; CI: 0.94-3.27).

Assessing the nature of the differences in the polymorphic loci of the cytokine gene interleukin IL17A (rs2275913) between groups of AIHA patients with moderate severity and healthy ones, a weak tendency was established to increase the frequency of occurrence of the weakened A allele by 1.6 times (20.0% versus 13.4%; $\chi2=2.3$; P=0.2; OR =1.6; CI: 0.87-3.0) (Table 3).

Table 3

Assessment of the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the pro-inflammatory cytokine interleukin IL17A (rs2275913) in the group of patients with moderate AIHA compared to healthy people.

Alleles and genotypes	Number of alleles and genotypes in groups				χ^2	P	RR	95%CI	OR	95%CI
	Group II		Group IV							
	n	%	n	%						
G	88	80.0	168	86.6	2.3	0.2	0.9	0.46 - 1.84	0.6	0.33-1.15
A	22	20.0	26	13.4	2.3	0.2	1.1	0.63 - 1.86	1.6	0.87-3.0
G/G	35	63.6	72	74.2	1.9	0.2	0.9	0.37 - 1.97	0.6	0.3-1.24
G/A	18	32.7	24	24.7	1.1	0.3	1.3	0.56 - 3.11	1.5	0.72-3.06
A/A	2	3.6	1	1.0	1.2	0.3	3.5	0.7 - 17.9	3.6	0.37-35.2

In parallel, in the distribution of the main G/G (63.6% versus 74.2%; $\chi2=1.9$; P=0.2; OR=0.6; CI: 0.3-1.24), as well as weakened G/A (32.7% versus 24.7%; $\chi2=1.1$; P=0.3; OR=1.5; CI: 0.72-3.06) and A/A (3.6% versus 1.0%; $\chi2=1.2$; P=0.3; OR=3.6; CI: 0.37-35.2) genotypes were not observed between the studied groups statistically significant differences.

Analyzing the degree of significance of differences in the carriage of alleles and genotypes of the cytokine polymorphic gene interleukin IL17A (rs2275913) in the group of patients with severe AIHA compared with healthy ones, it was established that there was a statistically highly significant increase in the frequency of the weakened A allele by 3.0 times (31.6% versus 13.4%; $\chi2= 12.0$; P=0.01; OR=3.0; CI: 1.61-5.54) (Table 4).

Table 4

Assessment of the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the pro-inflammatory cytokine interleukin IL17A (rs2275913) in the group of patients with severe AIHA compared to healthy people.

Alleles and	Number of alleles and genotypes in groups		χ^2	P	RR	95%CI	OR	95%CI
	Group III	Group IV						

	n	%	n	%						
G	52	68.4	168	86.6	12.0	0.01	0.8	0.38-1.64	0.3	0.18-0.62
A	24	31.6	26	13.4	12.0	0.01	1.3	0.74-2.17	3.0	1.61-5.54
G/G	18	47.4	72	74.2	8.9	0.01	0.6	0.23-1.79	0.3	0.15-0.67
G/A	16	42.1	24	24.7	3.9	0.05	1.7	0.61-4.78	2.2	1.01-4.84
A/A	4	10.5	1	1.0	6.9	0.01	10.2	3.65-28.6	11.3	1.85-68.9

Furthermore, statistically significant differences were found in the carrier of the two weakened genotypes G/A (42.1% vs. 24.7%; $\chi2=3.9$; P=0.05; OR=2.2; CI: 1.01– 4.84) and A/A (10.5% vs. 1.0%; $\chi2=6.9$; P=0.01; OR=11.3; CI: 1.85–68.9), their Transport increased the risk of severe AIHA by 2.2 and 11.3 times, respectively.

The results of the distribution of polymorphic loci of the cytokine gene interleukin IL-17F (rs763780) in healthy people (n=97) made it possible to determine the proportion of major His and weakened Arg alleles in 94.3% and 5.7% of the cases.

In the same group, as shown above, the frequencies of only two genotypes of the main His/His and the heterozygous His/Arg were determined, the frequencies of which were determined in 88.7% and 11.3% of cases, respectively (see Table 4.31).

Table 4.31

The nature of distribution of polymorphic loci of the polymorphism of the proinflammatory cytokine gene interleukin IL-17F (rs763780) in groups of patients with AIHA and healthy people.

Groups surveyed	Allele occurrence				Occurrence of genotypes					
	His		Arg		His/His		His/Arg		Arg/Arg	
	n	%	n	%	n	%	n	%	n	%
I main group AIHA, (n=93)	167	89.8	19	10.2	74	79.6	19	20.4	0	0.0
II – group AIHA with moderate to severe course, (n=55)	100	90.9	10	9.1	45	81.8	10	18.2	0	0.0
Group III AIHA with severe course, (n=38)	67	88.2	9	11.8	29	76.3	9	23.7	0	0.0
IV – comparison group of healthy people, (n=97)	183	94.3	11	5.7	86	88.7	11	11.3	0	0.0

The analysis carried out in the main group of AIHA compared with the healthy group showed a tendency towards an almost twofold increase in the mutant Arg allele (10.2% versus 5.7%; $\chi2=2.7$; P=0.2; OR=1.9; CI: 0.88-4.05).

Along with these features, a tendency was also established in the frequency of His/Arg heterozygotes, which among patients (20.4% versus 11.3%; $\chi2=3.0$; P=0.1; OR=2.0; CI: 0.91-4.45) was higher in comparison with healthy people. 2.0 times (see Table 4.32).

Table 4.32

Assessment of the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the pro-inflammatory cytokine interleukin IL-17F (rs763780) in the main group of patients with AIHA in relation to healthy people.

Alleles and genotypes	Number of alleles and genotypes in groups				χ^2	P	RR	95%CI	OR	95%CI
	Group I		Group IV							
	n	%	n	%						
His	167	89.8	183	94.3	2.7	0.2	1.0	0.54-1.69	0.5	0.25-1.13
Arg	19	10.2	11	5.7	2.7	0.2	1.1	0.41-2.7	1.9	0.88-4.05
His/His	74	79.6	86	88.7	3.0	0.1	0.9	0.48-1.68	0.5	0.22-1.1
His/Arg	19	20.4	11	11.3	3.0	0.1	1.8	0.96-3.37	2.0	0.91-4.45

The data obtained show an association between polymorphic loci of the cytokine polymorphic gene interleukin IL-17F (rs763780) and an increased risk of AIHA.

When assessing the nature of the differences in the polymorphic loci of the cytokine gene interleukin IL-17F (rs763780) between the groups of patients with moderate AIHA and healthy patients, it was found that there were no statistically significant differences in the proportions of the weakened Arg allele (9.1% vs. 5.7%; $\chi2 = 1.3$; P = 0.3; OR = 1.7; CI: 0.69–4.02) and His/Arg heterozygotes (18.2% versus 11.3%; $\chi2 = 1.4$; P = 0.3; OR = 1.7; CI: 0.69-4.37), although their proportion increased 1.7-fold compared to healthy ones (see Table 4.33).

Table **4.33**

Assessment of the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the pro-inflammatory cytokine interleukin IL-17F (rs763780) in the group of patients with moderate AIHA compared to healthy people.

Alleles and genotypes	Number of alleles and genotypes in groups				χ^2	P	RR	95%CI	OR	95%CI
	Group II		Group IV							
	n	%	n	%						
His	100	90.9	183	94.3	1.3	0.3	1.0	0.38 - 2.45	0.6	0.25-1.45
Arg	10	9.1	11	5.7	1.3	0.3	1.0	0.46 - 2.35	1.7	0.69-4.02
His/His	45	81.8	86	88.7	1.4	0.3	0.9	0.34 - 2.49	0.6	0.23-1.45
His/Arg	10	18.2	11	11.3	1.4	0.3	1.6	0.59 - 4.33	1.7	0.69-4.37

The differences between the unfavorable allele (Arg) and the genotype (His/Arg) of the cytokine polymorphic gene of interleukin IL-17F (rs763780) in the group of patients with severe AIHA compared to healthy patients showed a clear tendency to increase or decrease 2.2 (11.8% vs. 5.7%; $\chi2 = 3.0$; P = 0.1; OR = 2.2; CI: 0.9–5.52) and 2.4-fold (23.7% versus 11.3%; $\chi2 = 3.3$; P = 0.1; OR = 2.4; CI: 0.93). -6.32) (see Table 4.34).

Table 4.34

To evaluate the significance of differences in the proportions of alleles and genotypes of the polymorphic gene of the proinflammatory cytokine interleukin IL-17F (rs763780) in the group of patients with severe AIHA compared to healthy people.

Alleles and genotypes	Number of alleles and genotypes in groups				χ^2	P	RR	95%CI	OR	95%CI
	Group III		Group IV							
	n	%	n	%						
His	67	88.2	183	94.3	3.0	0.10	0.9	0.33-2.62	0.5	0.18-1.11
Arg	9	11.8	11	5.7	3.0	0.10	1.1	0.49-2.36	2.2	0.9-5.52
His/His	29	76.3	86	88.7	3.3	0.10	0.9	0.28-2.67	0.4	0.16-1.07
His/Arg	9	23.7	11	11.3	3.3	0.10	2.1	0.67-6.48	2.4	0.93-6.32

When comparing the differences between allele frequencies (Arg: 9.1% vs. 11.8%; $\chi2 = 0.4$; P = 0.6; OR = 0.7; CI: 0.29–1.92) and genotypes (His/Arg: 18.2% vs. 23.7%) ; $\chi2 =0.4$; P=0.6; OR=0.7; CI: 0.26-1.97) of the cytokine polymorphic interleukin gene IL-17F (rs763780) in groups of patients with moderate and severe AIHA, no statistically significant values were identified, this was due to their relatively similar proportions in both study groups.

Conclusion.

Autoimmune hemolytic anemia (AIHA) is a rare pathology; the incidence in the general population is 1–3 cases per 100,000 inhabitants [5, 7]. AIHA occurs in every age group, but the incidence has been found to increase with age [10,13].

According to modern ideas about the pathogenesis of AIHA, the development of autoimmune diseases is the result of a complex interaction of genetic predisposition factors and the environment [5]. In AIHA in particular, as in other autoimmune diseases, a connection with genetic factors has been found [7, 8, 11, 14, 15].

The basis for conducting this study was the lack of data on the role of IL17A (rs2275913) and IL17F (rs763780) in increasing the risk of developing the disease and its severe course in the Uzbek population.

As a result of this study, we examined the nature of the differences in the distribution of alleles and genotypes of the cytokine polymorphic gene interleukin IL17A (rs2275913) in the main group of patients with AIHA compared to healthy patients and found that the carriers of a weakened allele (A) and weakened genotypes (G/A and A/A) are 2.1-fold ($\chi2=7.9$; P=0.01), 1.8-fold ($\chi2=3.1$; P=0.1) and 6.6 times increased risk of AIHA ($\chi2=3.9$; P=0.05).

In the distribution of alleles and genotypes of the cytokine polymorphic interleukin gene IL17A (rs2275913) in the group of patients with severe AIHA compared to healthy individuals, it was found that the weakened allele (A) and genotypes (G/A and A /A) are statistically significant with a fold of 3.0 ($\chi2=12.0$; P=0.01), 2.2 fold ($\chi2=3.9$; P=0.05) and 11, 3-fold ($\chi2=6.9$; P=0.01) increased risk of developing this form of AIHA.

Consequently, the polymorphic interleukin gene IL17A (rs2275913) is statistically significantly associated with an increased risk of developing AIHA and its severe course.

Statistical calculations of the distribution of polymorphic loci of the cytokine polymorphic gene interleukin IL-17F (rs763780) in patient groups compared to healthy patients made it possible to establish the presence of a tendency to increase the risk of developing AIHA in carriers of the mutant Arg allele almost twice as much ($\chi2$ = 2.7; P = 0.2) and His/Arg heterozygous carriers twice as much (20.4% versus 11.3%; $\chi2$ = 3.0; P = 0.1; OR = 2.0; CI: 0.91–4.45) and a trend toward a 2.2-fold ($\chi2$=3.0; P=0.1) and 2.4-fold ($\chi2$=3.3; P=0.1) increased risk for development, respectively severe AIHA when unfavorable alleles (Arg) and genotype (His/Arg) are carried, respectively.

Consequently, the polymorphic interleukin gene IL-17F (rs763780) can be considered a genetic factor playing a role in the development of this pathology due to its possible involvement in increasing the risk of AIHA and its severe course.

Thus, the results show the possible contribution of the polymorphic genes IL17A (rs2275913) and IL-17F (rs763780) to the mechanisms of AIHA development and the development of severe diseases.

References:

1. Васильченкова П.И., Гальцева И.В., Лукина Е.А. Аутоиммунная гемолитическая анемия: современное состояние вопроса // ОГ. 2023. №2. URL: https://cyberleninka.ru/article/n/autoimmunnaya-gemoliticheskaya-anemiya-sovremennoe-sostoyanie-voprosa.
2. Жахонов А. Х., Саидов А. Б., Маткаримова Д. С. Вклад полиморфного гена IL17A (rs2275913) в механизмы формирования аутоиммунной гемолитической анемии //Наука и инновация. – 2023. – Т. 1. – №. 15. – С. 77-78.
3. Жахонов А. Х., Саидов А. Б., Маткаримова Д. С. Лабораторные проявления у больных с аутоиммунной гемолитической анемией //Евразийский журнал медицинских и естественных наук. – 2023. – Т. 3. – №. 12. – С. 28-34.
4. Маткаримова Д.С., Каримов Х.Я., Бобоев К.Т. Связь некоторых генов провоспалительных цитокинов с риском развития иммунного микротромбоваскулита // Вестник гематологии. 2022. №2. URL: https://cyberleninka.ru/article/n/svyaz-nekotoryh-genov-provospalitelnyh-tsitokinov-s-riskom-razvitiya-immunnogo-mikrotrombovaskulita.
5. Barcellini W. New insights in the pathogenesis of autoimmune hemolytic anemia //Transfusion medicine and hemotherapy. – 2015. – Т. 42. – №. 5. – С. 287-293.
6. Barcellini W., Giannotta J., Fattizzo B. Autoimmune hemolytic anemia in adults: primary risk factors and diagnostic procedures //Expert Review of Hematology. – 2020. – Т. 13. – №. 6. – С. 585-597
7. Berentsen S., Barcellini W. Autoimmune hemolytic anemias //New England Journal of Medicine. – 2021. – Т. 385. – №. 15. – С. 1407-1419.
8. Elkoumi M. A. et al. Association of interleukin-17A gene polymorphisms and susceptibility to systemic lupus erythematosus in Egyptian children and adolescents: a multi-centre study //Lupus. – 2020. – Т. 29. – №. 7. – С. 767-775.
9. Fattizzo B., Barcellini W. Autoimmune hemolytic anemia: causes and consequences //Expert Review of Clinical Immunology. – 2022. – Т. 18. – №. 7. – С. 731-745.

10. Kandinata S. G., Soelistijo S. A., Amrita P. N. A. Graves' disease presenting as autoimmune hemolytic anemia //The American Journal of Case Reports. – 2021. – Т. 22. – С. e930705-1.
11. Karimov H. Y., Matkarimova D. S., Boboev K. T. Allelic polymorphism of the IL-1β (rs1143627) gene in patients with immune thrombocy th immune thrombocytopenia. – 2021.
12. Karki P. et al. Autoimmune Hemolytic Anemia with Autoimmune Hypothyroidism: A Case Report //JNMA: Journal of the Nepal Medical Association. – 2023. – Т. 61. – №. 263. – С. 614.
13. Khanmohammadi S. et al. Lymphoma in the setting of autoimmune diseases: a review of association and mechanisms //Critical Reviews in Oncology/Hematology. – 2020. – Т. 150. – С. 102945.
14. Michalak S. S. et al. Autoimmune hemolytic anemia: current knowledge and perspectives //Immunity & Ageing. – 2020. – Т. 17. – №. 1. – С. 1-16.
15. Sirianni M. F. M. et al. HLA-DRB1 and cytokine polymorphisms in Brazilian patients with myelodysplastic syndromes and its association with red blood cell alloimmunization //Transfusion Medicine. – 2022. – Т. 32. – №. 5. – С. 394-401.
16. Zaninoni A. et al. Cytokine polymorphisms in patients with autoimmune hemolytic anemia //Frontiers in Immunology. – 2023. – Т. 14.
17. Zaninoni A. et al. Single Nucleotide Polymorphisms of Cytokine Genes in Warm Autoimmune Hemolytic Anemias: Relationship with Clinical and Hematological Parameters //Blood. – 2021. – Т. 138. – С. 4142.